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METHODS: We tested three sets of reagents as follows: (1) in-tem and ex-tem (Tem International GmbH); (2) kaolin and RapidTEG (Haemonetics); (3) a well-characterized control recombinant tissue factorYphospholipid reagent. Blood was drawn from six healthy donors, and each reagent was run concurrently in the TEG and ROTEM instruments. The volume of commercial reagent and calcium used was adjusted for crossover measurements to maintain the same concentration of each reagent in the blood. The outputs of clot time, rate of clot formation, and maximum firmness of the clot of the ROTEM and the TEG tracings were evaluated.
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Block 13: Supplementary Note

Interchangeability of rotational elastographic instruments and reagents

Maya Aleshnick, BS, Thomas Orfeo, PhD, Kathleen Brummel-Ziedins, PhD, Matthew Gissel, MS, *and* **Kenneth Mann, PhD,** *Colchester, Vermont*

BACKGROUND: Viscoelastic measurements are frequently being used in clinical and research settings for a rapid assessment of the hemostatic processes of blood clot formation and degradation. These measurements are being performed on either of two instruments (TEG and ROTEM) using their proprietary reagents. Standardization between the instruments and the reagents has been lacking but is necessary to compare results across instruments. In this study, we perform a crossover analysis between the TEG and ROTEM instruments using proprietary reagents from each manufacturer.

METHODS: We tested three sets of reagents as follows: (1) in-tem and ex-tem (Tem International GmbH); (2) kaolin and RapidTEG (Haemonetics); (3) a well-characterized control recombinant tissue factor–phospholipid reagent. Blood was drawn from six healthy donors, and each reagent was run concurrently in the TEG and ROTEM instruments. The volume of commercial reagent and calcium used was adjusted for crossover measurements to maintain the same concentration of each reagent in the blood. The outputs of clot time, rate of clot formation, and maximum firmness of the clot of the ROTEM and the TEG tracings were evaluated.

RESULTS: The in-tem and RapidTEG reagents showed no disparity between instruments for any parameter. Significant differences between the instruments were found in the α angle and maximum firmness of the clot for ex-tem and kaolin reagents as well as in the clot time and maximum firmness of the clot for the recombinant tissue factor–phospholipid reagent.

CONCLUSION: Although significant differences were observed for some parameters, the magnitudes were small compared with the differences between tests or the normal range variation in parameter values observed for these tests. These findings indicate that the instruments are more interchangeable than previously reported. (*J Trauma Acute Care Surg*. 2014;76: 107–113. Copyright © 2014 by Lippincott Williams & Wilkins)

KEY WORDS: TEG; ROTEM; crossover comparison; viscoelastic measurements; blood coagulation.

Viscoelastic measurements are increasingly being used in emergency departments, surgical sites, and research laboratories throughout the world[1] owing to their ability to provide a relatively fast and multifaceted assessment of hemostatic processes. The overall importance of viscoelastic measurements in the management of trauma,[2–5] cardiac surgery,[3,6,7] liver transplantations,[3,7] obstetrics,[1,3,7] and other conditions[1,3,5,7] has been reviewed recently. Such measurements have also been used to study coagulation dynamics in a variety of nonclinical situations.[8–13]

The viscoelastic technique reports the formation and degradation of the platelet-fibrin clot in phlebotomy blood exposed to a protein initiator or initiating surface. Changes in blood viscosity caused by the formation and later degradation of the platelet-fibrin clot are measured mechanically over time, providing quantitative measures that describe the overall coagulation process. These parameters display properties of the blood with little delay and more recently are used in some clinical settings to direct treatment. Some of the parameters of this technique have been shown to correlate directly to thrombin generation assays[14] and other traditional coagulation tests (reviewed by Sankarankutty et al.[15]), while correlating other thrombotic parameters has been more problematic.[14,16]

The instruments commercially available to measure the viscoelastic properties of clot formation and lysis in whole blood are the TEG (Haemonetics, Braintree, MA) and the ROTEM (Tem International GmbH, Munich, Germany). Both instruments are being used in clinical settings. A comparison of the measurement principles of the instruments as well as the most commonly used clinically relevant parameters have been reported previously.[11] Each supplier offers an array of tests containing various activators and inhibitors that allow for the assessment of specific hemostatic parameters. A compilation of the tests that are commercially available for both instruments is presented in Table 1. Although some tests available from the two manufacturers are similar, there is no complete overlap in the tests available for each instrument and, because of this, some hemostatic processes cannot be assessed in one or the other instrument.

A concern regarding the use of the TEG and ROTEM in clinical and research settings is whether the instruments are interchangeable in evaluating patient populations. Several reviews have recently been published addressing this issue. One review by Sankarankutty et al.[15] searched the literature for comparisons of TEG with ROTEM and found only four such studies, which did not support what they characterized as

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TABLE 1. Commercially Available Tests From Haemonetics and Tem International GmbH

Characterized Parameter	Tem International (ROTEM) Assay	Haemonetics (TEG) Assay
Intrinsic pathway initiated coagulation	Initiator: ellagic acid (in-tem)	Initiator: kaolin
Extrinsic pathway initiated coagulation	Initiator: tissue factor (ex-tem)	—
Combination intrinsic/extrinsic pathway initiated coagulation	—	Initiator: kaolin + tissue factor (RapidTEG)
Fibrinogen levels	Platelet inhibitor: cytochalasin D (fib-tem)	Platelet inhibitor: abciximab (Functional Fibrinogen)
Effects of heparin	Heparinase added to sample (hep-tem)	Heparinase-treated cups/pins
Fibrinolytic effects	Aprotinin added to sample (ap-tem)	—
Platelet function	—	PlateletMapping
Native blood	11.8-mM Ca2+ to recalcify (na-tem)	11.1-mM Ca2+ to recalcify

a "prevalent opinion" that the instruments are interchangeable in results and subsequent interpretations. The relative equivalence of commonly used reagents for TEG and ROTEM, when used in the instrument for which they are designed, has been assessed in trauma and cardiac surgery patients,[17–19] and the clinical indications for the treatment resulting from the analysis with TEG and ROTEM instruments and their proprietary tests have been compared.[20] These studies have not found the systems to be interchangeable. However, these studies have not taken into account differences in the intensity of the stimulus between the compared reagents. The relationship between stimulus magnitude and the discriminating power of a global hemostasis assay is well documented and has been explored in depth for the thrombogram technology. For example, the ability both to identify deficiencies in factor VIII (FVIII)[21] and to observe the effects of FXI activation on clot formation[22] have been shown to be dependent on the magnitude of the tissue factor stimulus. The varying nature and strength of the activators is a limitation in the ability to make direct comparisons between instruments that has been highlighted by the TEG-ROTEM Working Group, which concluded that the results from the instruments are not comparable owing to the differences between the activators.[11]

One study conducted by Solomon et al.[23] attempted to overcome this concern by normalizing the activator stimulus in a crossover study between reagents and instruments using fib-tem (ROTEM reagent) and Functional Fibrinogen (TEG reagent). The authors conclude that neither the instruments nor the tests are interchangeable with regard to the maximum clot firmness (MCF, ROTEM parameter) and maximum amplitude (MA, corresponding TEG parameter). Other parameters were not assessed in this study. In another study, the instruments were compared using a series of pooled plasmas activated by celite, with the concentration of celite remaining constant across machines.[24] The instruments were found to produce similar results in the presence of a celite activator; however, significant differences were found between the instruments in the absence of a exogenous activator. This may reflect the fact that different plastic materials are used in the TEG and ROTEM cups, presumably resulting in differences in the dynamics of contact activation.

The relative equivalence of the TEG and ROTEM instruments in assessing whole blood hemostasis using the tests frequently used in clinical settings has not been established. The need for such a study has been expressed repeatedly.[2,11,15] This study compares the outputs of the instruments when used with five tests, two from each manufacturer along with a control activator, a well-characterized tissue factor–phospholipid reagent.[25] We have previously reported the reproducibility in TEG of a similar standardized tissue factor reagent constructed from purified recombinant tissue factor and synthetic phospholipids.[26] Such a study will establish whether the reagents can reliably be interchanged between instruments. If a list of tests universal to both instruments is established, the versatility of both TEG and ROTEM will be increased.

PATIENTS AND METHODS

Subjects

Six healthy volunteers (three female and three male subjects) with a normal coagulation history aged 23 years to 34 years were recruited and advised according to a protocol approved by the institutional review board of the University of Vermont Human Studies Committee. Informed written consent was obtained from all subjects before blood collection.

Blood Sampling

Blood was drawn via phlebotomy using a 19 3/4 gauge butterfly needle from an anticubital vein into citrate tubes containing 3.2% sodium citrate, resulting in a 10% dilution of the blood. The tubes were immediately inverted three to four times after draw and kept at 37°C until use; the first tube was discarded to avoid contamination by tissue factor at the site of the needle stick. All blood sampling was performed by the same phlebotomist.

Reagents

In-tem and ex-tem reagents were purchased from Tem Systems, Inc. (Durham, NC). Kaolin and RapidTEG reagents were purchased from Haemonetics. All commercial reagents were prepared as per the recommendation of the manufacturer, including reconstitution (RapidTEG only), warming from storage temperature (all), and the use before expiration date. The recombinant tissue factor (residues 1–263 [$rTF_{1–263}$]) was a gift from Haematologic Technologies (Essex Junction, VT) and was relipidated in PCPS (75% PC/25% PS) vesicles as by a previously described protocol.[25,27] $rTf_{1–263}$ was diluted to the required intermediate dilution (85 pM for ROTEM and

90 pM for TEG) in 20-mM HEPES, 150-mM NaCl, pH 7.4, immediately before transfer to the cups. The final concentration of rTf_{1-263} in the blood was held constant at 5 pM.

Instruments

Three 2-channel TEG 5000 Thrombelastograph Hemostasis Analyzers and two 4-channel ROTEM Delta Analyzers were used. The ROTEM instruments were quality controlled within 7 days of performing any experiment per manufacturer's instructions, using in-tem/ex-tem activators and the proprietary lyophilized plasma (ROTROL-N). Output parameters were within the acceptable range designated by the manufacturer. During the period during which the experiments were conducted, a total of 18 quality control tests were run on the TEG, and all output parameters were within the acceptable range. The means and SDs for the TEG parameters using the Level 1 control are as follows: *R* time, 0.96 minutes with an SD of 0.13 minutes (acceptable range is 0–3 minutes); *K* time, 0.83 minutes with an SD of 0 minutes (acceptable range is 0–2 minutes); α angle, 84.6 degrees with an SD of 0.5 degrees (acceptable range is 76–88 degrees); MA, 51.2 mm with an SD of 2.4 mm (acceptable range is 38–58 mm).

Study Design

TEG and ROTEM outputs were compared using four commercially available reagents (in-tem, ex-tem, kaolin, and RapidTEG) as well as a characterized tissue factor reagent (rTf_{1-263}). For each reagent examined, the assay method and calcium source suggested by the manufacturer of the reagent were used in all instruments. Volume adjustments were made to the calcium, activator, and citrate blood additions to maintain the same concentrations of these components in each instrument, to compensate for the difference in the manufacturer-recommended final volume (340 μL for ROTEM and 360 μL for TEG). To establish the same concentration of calcium and activator in the blood using the commercial reagents, the volume of blood could not be kept absolutely constant across tests. The volumes of activator and calcium and the percentage of blood in each assay are reported in Table 2.

Each of the five reagents was run concurrently in both instruments with blood obtained from a single draw. Blood sampling was performed twice on each donor to run the tests because channel limitations did not allow for duplicates of all five tests to be run from a single draw. The in-tem, ex-tem, and rTf_{1-263} tests were run using blood from the first draw, and the kaolin and RapidTEG tests were run using blood from a second draw. Draws from all six donors were performed within a 3-week period. All assays were performed by the same technician. The automatic pipette provided with the ROTEM was not used for this study to ensure similar treatment of samples for both instruments.

Viscoelastic Measurements

All reagents to be spotted into cups were added before blood draw. All tests were initiated by pipetting citrated blood into the cup and mixing three times by aspirating into the pipette once and slowly dispensing it. The thromboelastographic recording was started immediately after the carrier was raised and, in the TEG, the control lever was moved to "test." All conditions were performed in duplicate and were started within 10 minutes of needle stick. The amount of time citrate blood "sits" before viscoelastic analysis is a subject of discussion.[11] In this study, the tests were started within 10 minutes of needle stick to mimic one scenario typical of a clinical setting. Preliminary experiments in our laboratory have indicated that when citrate blood is assayed 45 minutes after draw, the pattern of instrument responses to the various activators is consistent to that seen at less than 10 minutes (data not shown).

Four variables were measured in each instrument. The clot time (CT), MCF, and α angle, a measure of clot formation rate, are ROTEM parameters corresponding to the reaction time (*R*), MA, and α angle in the TEG, respectively. The *G* value, or shear elastic modulus strength, is a parameter calculated by both instruments using the expression $5{,}000 \times (\mathrm{MA} / \mathrm{MCF}) / 100 - (\mathrm{MA} / \mathrm{MCF})$.[28,29]

TEG Assays

For kaolin and RapidTEG trials, 20 μL of 0.2-M $CaCl_2$ (reagent provided by Haemonetics) was spotted into cups. For RapidTEG trials, 10 μL of RapidTEG reagent was added to the cups, followed by 330 μL of citrated blood (Table 2). For kaolin trials, 1 mL of citrated blood was pipetted into the kaolin vial and inverted five times, after which 340 μL was added to a cup containing calcium. For in-tem and ex-tem trials, 21.2 μL each of star-tem and in/ex-tem was spotted into the cups, followed by 318 μL of citrated blood. For rTf_{1-263}

TABLE 2. Composition of Blood/Activator Mixtures

	ROTEM Instrument Volume, μL					TEG Instrument Volume, μL				
	Citrate Blood	Calcium	Activator	Total Volume	Citrate Blood, %	Citrate Blood	Calcium	Activator	Total Volume	Citrate Blood, %
in-tem	**300**	**20***	**20**	340	88	318	21.2*	21.2	360	88
ex-tem	**300**	**20***	**20**	340	88	318	21.2*	21.2	360	88
Kaolin	309	18.9**	12.3	340	91	**327**	**20****	**13**	360	91
RapidTEG	312	18.9**	9.44	340	92	**330**	**20****	**10**	360	92
rTf_{1-263}	300	20†	20	340	88	320	20‡	20	360	89

*Star-tem reagent provided by Tem Systems, containing 0.2-M calcium.
**Calcium reagent provided by Haemonetics, containing 0.2 M calcium.
†Prepared stock of 0.255-M calcium dihydrate solution.
‡Prepared stock of 0.27-M calcium dihydrate solution.
Parameter values in bold represent noncrossed conditions (e.g., ROTEM reagents in ROTEM instrument).

TABLE 3. Assay Outputs for TEG and ROTEM Crossover Study

	CT/R, min		α Angle, degree		MCF/MA, mm	
Assay	**ROTEM**	**TEG**	**ROTEM**	**TEG**	**ROTEM**	**TEG**
in-tem	2.60 (0.07)	2.54 (0.18)	75.67 (1.29)	75.53 (1.83)	61.50 (1.22)	63.00 (1.55)
ex-tem	0.80 (0.08)	0.74 (0.03)	72.42 (0.65)	74.63 (1.39)	59.58 (1.12)	63.18 (0.91)
Kaolin	9.91 (0.68)	10.26 (0.56)	59.42 (3.28)	55.78 (3.46)	58.17 (1.35)	59.83 (1.46)
RapidTEG	0.89 (0.09)	0.78 (0.06)	71.17 (2.08)	71.04 (0.81)	61.33 (1.22)	62.18 (1.15)
rTf_{1-263}	8.24 (0.28)	7.98 (0.38)	62.12 (3.34)	61.66 (1.34)	57.75 (1.32)	62.39 (1.40)

Data represent mean (SD) (n = 6).

trials, 20 μL of 90-pM rTf_{1-263} and 20 μL of 0.27-M $CaCl_2$ was spotted into the cups, followed by 320 μL of citrated blood, achieving a final rTf_{1-263} concentration of 5 pM.

ROTEM Assays

For kaolin and RapidTEG trials, 18.9 μL of 0.2-M $CaCl_2$ (reagent provided by Haemonetics) was spotted into cups. For RapidTEG trials, 9.44 μL of RapidTEG reagent was added to the cups, followed by 312 μL of citrated blood (Table 2). For kaolin trials, 321 μL of kaolin-activated citrated blood (as described earlier) was added to cups containing calcium. For in-tem and ex-tem trials, 20 μL each of star-tem and in/ex-tem was spotted into the cups, followed by 300 μL of citrated blood. For rTf_{1-263} trials, 20 μL of 85-pM rTf_{1-263} and 20 μL of 0.255-M $CaCl_2$ was spotted into the cups, followed by 300 μL of citrated blood, achieving a final rTf_{1-263} concentration of 5 pM.

Statistical Analyses

All data are expressed as the mean (SD) of duplicate determinations. A mixed-model analysis of variance was used to compare differences between machines. A two-tailed $p < 0.05$ was used to indicate a significant difference.

RESULTS

Normalizing Activators Between Instruments

The percentage of citrate blood in the total volume of the cup was constant between instruments for the same test and ranged between 88% and 92% across tests (Table 2). Thus, the levels of fibrinogen, platelets, red blood cells, and other coagulation factors did not vary between instruments for the same test for a given individual and only marginally between tests.

Comparison of Instrument Outputs With Crossed Over Reagents

Experiments were performed using the normalized reagent crossover design described in the Patients and Methods section. Initially, three viscoelastic output parameters were assessed as follows: the time to reach 2-mm amplitude (CT for

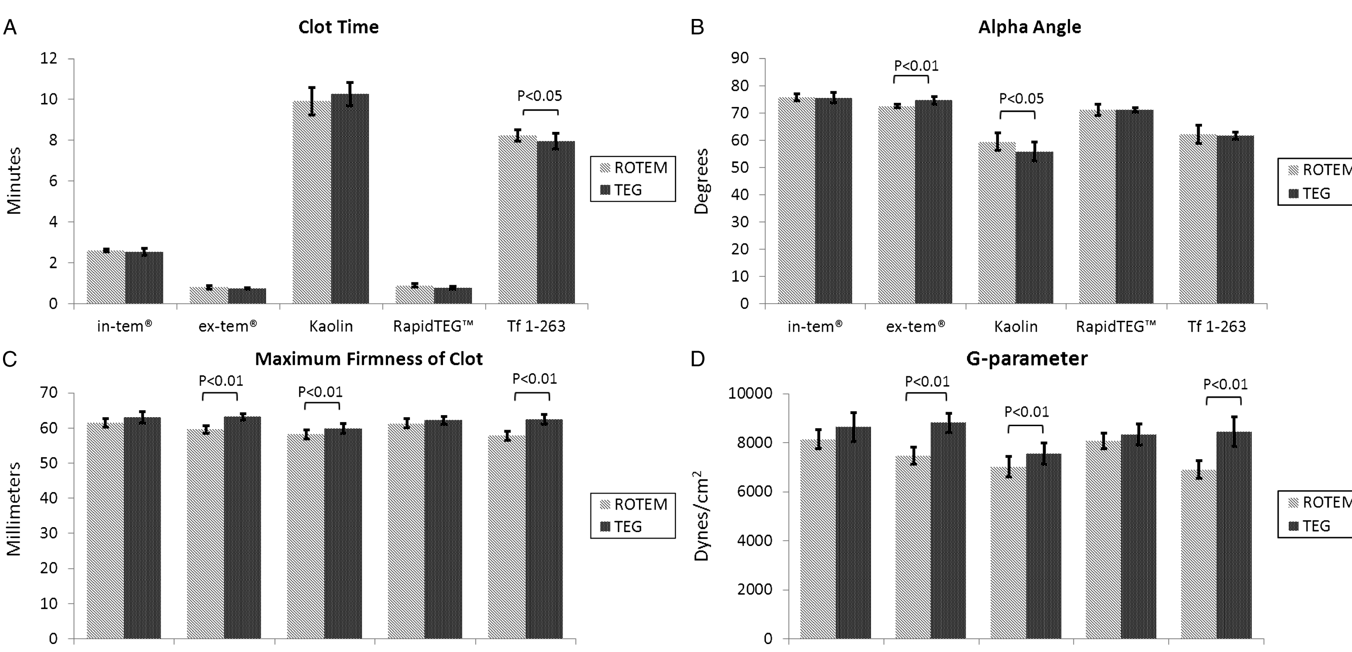

Figure 1. Comparison of ROTEM and TEG outputs for the five initiators. The data are presented as the mean (SD) (n = 6) for each parameter. Significant difference ($p < 0.05$) between ROTEM and TEG derived parameter values are indicated. *A*, CT. *B*, α angle. *C*, maximum firmness of clot. *D*, *G* parameter (sheer elastic modulus strength).

ROTEM and *R* time for TEG), the kinetics of clot formation (α angle for both machines, Chitlur and Lusher[11] for a thorough description of α angle determination), and the maximum firmness of the clot (MCF for ROTEM and MA for TEG). The data are summarized in Table 3 and Figure 1*A* to *C*, which illustrates the output parameter comparisons between TEG and ROTEM for the five reagents.

All three parameters for the in-tem test were not significantly different between the instruments ($p > 0.1$). All three parameters for the RapidTEG test were not significantly different between the instruments ($p > 0.05$).

The CT parameter showed no difference between instruments for the ex-tem test. Both α angle and MCF/MA were significantly different between instruments in the ex-tem test ($p < 0.001$), with the TEG showing a faster rate of clot formation and reaching a greater maximal amplitude. The difference between average TEG MA and average ROTEM MCF was 3.6 mm, and the difference between α angles was 2.2 degrees. When directly comparing each individual donor, the average of duplicate MCF (ROTEM) values was between 92% and 95% of the average MA (TEG) values.

For the kaolin assay, the CT parameter showed no difference between instruments. Both the α angle and MCF/MA values were significantly different. Although significant, the differences between MCF/MA averages were less than 2 mm, while SDs were greater than 1 mm for both data sets. The TEG average yielded higher MA value. When considering each individual donor, the average of duplicate MCF (ROTEM) values was between 95% and 100% of the average TEG MA value. The α angles were also statistically different, with a difference between averages of 6.34 degrees. The SD of each data set was greater than 3 degrees, with the ROTEM showing a faster rate of clot formation.

The $rTf_{1–263}$ reagent was the only test that showed a difference in CT, with the average ROTEM CT falling 16 seconds after the average TEG CT. The SD for both of these data sets is greater than this difference. MCF/MA was also different in the $rTf_{1–263}$ assay ($p < 0.001$); however, the α angle was not. When considering each individual donor, the average of duplicate MCF (ROTEM) values was between 89% and 95% of the average MA (TEG) values.

Although the MA/MCF parameter is frequently used clinically, the *G* parameter, the shear elastic modulus strength, seems to be a more sensitive measure of small changes in clot firmness.[28] An analysis of the variance between instruments in *G* values for each reagent is presented in Figure 1*D*. The results do not differ from those based on the MCF/MA parameter.

DISCUSSION

This study is the first crossover analysis comparing the outputs of each instrument when used with the basic tests from each manufacturer. Comparing five reagents across the two instruments using phlebotomy blood from six donors, we have found that two of the reagents (the in-tem and the RapidTEG) are interchangeable for all parameters assessed. The response of the instruments to three of the reagents (ex-tem, kaolin, and $rTF_{1–263}$) differed in two of the three parameters assessed. The lack of interchangeability did not seem related to whether the

TABLE 4. Differences Between TEG and ROTEM Parameter Outputs Compared With Normal Range Variation in These Parameters

	α Angle, degree				MCF/MA, mm			
Assay	Normal Range	Average Output for ROTEM and TEG	Average Difference Between ROTEM and TEG	Maximum Difference Between ROTEM and TEG*	Normal Range	Average Output for ROTEM and TEG	Average Difference Between ROTEM and TEG	Maximum Difference Between ROTEM and TEG*
Ex-tem	63–81[30]	*R*: 72.42 *T*: 74.63	2.22	3.60	49–71[30]	*R*: 59.58 *T*: 63.18	3.60	5.75
Kaolin	55–78[28] 53–72[34] 47.8–77.7[31]	*R*: 59.42 *T*: 55.78	3.64	6.05	51–69[28] 50–70[34] 49.7–72.7[31]	*R*: 58.17 *T*: 59.83	1.66	2.95

*Most disparate individual with respect to TEG and ROTEM outputs.

activator worked through the extrinsic (rTf_{1-263} reagent, ex-tem) or intrinsic activation pathway (kaolin).

A number of publications have highlighted the discrepancies between TEG and ROTEM outputs in a variety of clinical environments[17,18,23,24] and the potential for these differences to result in conflicting recommendations for treatment.[20] Since the proprietary activators used to probe the dynamics of a blood sample differ in their pathway of activation (extrinsic or intrinsic) and in their formulation between the companies, a lack of interchangeability might seem noncontroversial. A thorough crossover analysis comparing the responses of the two instruments to the fib-tem (ROTEM) and Functional Fibrinogen (TEG) reagents showed a lack of interchangeability between reagents, consistent with this expectation, and also between instruments. Somewhat in contrast, Nielsen[24] reported that the two instruments displayed no significant differences in responses in 10 of 12 parameter comparisons when a series of test plasmas was initiated by a common activator, celite.

The kaolin and ex-tem reagents were shown to give nonequivalent responses in the two instruments in both α angle and MCF/MA parameters. However, given their relative magnitude (Table 4), the importance of these differences to clinical decision making is open to question. Table 4 compares the manufacturer-reported normal ranges for these activators in their respective instruments to both the average parameter values and the variance in parameter values between instruments observed in this study. The normal ranges for ROTEM tests were established in a multicenter study;[30] the analysis in this study indicated that the ROTEM measurements were normally distributed. Normal range values for TEG reagents are from the manufacturer.[28] Also reported are the ranges established by a study of 118 healthy volunteers, which the authors reported as varying significantly from the ranges reported by the manufacturer.[31]

The normal parameter ranges for the ex-tem reagent are 49 mm to 71 mm for the MCF and 63 degrees to 81 degrees for the α angle (Table 4). The maximum differences between instruments observed among the individuals tested were 5.75 mm for the MCF/MA and 3.60 degrees for the α angle. In both cases, the magnitude of each parameter's normal range is approximately fourfold greater than these instrument differences.

With the use of the kaolin reagent in the TEG, the normal range for the MA is 51 mm to 69 mm (Table 4). This 18-mm region defining the normal range of an apparently healthy population measured by the TEG instrument is approximately 10-fold greater than the average difference observed between instruments (1.66 mm) for our population and approximately 6-fold greater than the maximum difference observed in any individual donor (2.95 mm). Similarly with respect to the α angle parameter, the size of the normal range (55–78 degrees, Table 4) is much larger than the differences between instruments for the population (3.64 degrees) or that of the individual most disparate between instruments (6.05 degrees). Thus, to the extent that the distribution of normal parameter values is not concentrated disproportionately at the extremes of the ranges,[30] these analyses suggest that for many healthy individuals, these two reagents will be interchangeable between the instruments, that is, the chance of misidentifying a healthy individual as compromised will be small.

In contrast, conclusions concerning the likelihood of misidentifying coagulopathic individuals as normal when interchanging these reagents between instruments cannot be drawn from this study. Some data are available describing how individuals whose parameter responses to these activators fall outside the normal parameter range are distributed.[32,33] However, no crossover studies focused on populations expected to be outside the normal parameter ranges in their viscoelastic responses have been reported. Such studies would be necessary to demonstrate that the interchangeability of reagents and instruments extends to coagulopathic populations.

When developing global assays for clinical use, there is a fine balance between expediting the standardization process to allow for clinical use as early as possible and conducting the appropriate standardization experiments for testing the multiple variables that might affect parameter outcomes. The TEG and ROTEM instruments are starting to be more widely used in clinical and research settings, and now is the time to perform the vital harmonization and standardization of these viscoelastic assays.

AUTHORSHIP

M.A. performed the experiments and prepared the manuscript. T.O. assisted with the data analysis and interpretation as well as preparation of the manuscript. K.B.-Z. assisted with the data analysis and interpretation as well as preparation of the manuscript. M.G. assisted with the statistical analyses and data interpretation. K.M. designed the study, assisted with the data analysis and interpretation, as well as preparation of the manuscript.

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DISCLOSURE

Dr. Kenneth Mann is consultant to Daiichi-Sankyo, Merck, Baxter, GTI, Alnylam, and T2 Biosystems and chairman of the board of Haematologic Technologies, Inc. The other authors declare no conflict of interest.
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